Bioterrorism Agent Fact Sheet

Plague/*Yersinia pestis*

Disease

Naturally occurring plague is a zoonotic disease of rodents that can be transmitted by vector to humans. It is caused by the non-sporulating, gram-negative coccobacillus *Yersinia pestis*, a member of the Enterobacteriaceae family. Three plague pandemics have killed more than 200 million people, including the Black Death epidemics in 14th Century Europe. Large outbreaks are now rare, but cases of plague, primarily the bubonic form, still arise regularly in endemic areas (10-15 cases per year in the southwestern US). Pneumonic plague is considered one of the diseases most likely to be encountered in a bioterrorism event. Intentional aerosol release should be suspected if human cases occur in nonendemic areas and/or in persons with no risk factors. Outbreaks of any form of plague should be rapidly investigated to rule out a bioterrorism event. There are three forms of plague:

- **Pneumonic plague**
  Least common (< 14% of all cases), but most severe form characterized by fulminant pneumonia • termed *primary pneumonic plague* if acquired via respiratory tract and lacking buboes or *secondary pneumonic plague* if initially bubonic form complicated by hematogenous spread to lungs • overall mortality: 57% • The form most likely to be seen in a bioterrorism setting

- **Bubonic plague**
  Most common form (75-97% of all cases) • characterized by painful lymphadenitis (buboes) • contracted through the bite of an infected flea or handling infected animals • overall mortality: 15% • This form is unlikely to occur in a bioterrorism setting

- **Septicemic plague**
  Less common form (< 20% of all cases) • systemic infection characterized by high-grade bacteremia and sepsis • termed *primary septicemic plague* if no buboes are detected or *secondary septicemic plague* if developed as a complication of bubonic • overall mortality: 22-50%

Diagnosis

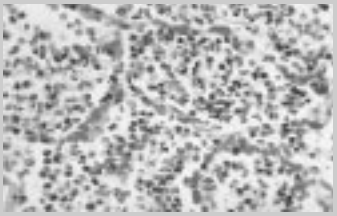
There are currently no widely available rapid confirmatory diagnostic tests. A presumptive diagnosis can be made quickly based on symptoms and concurrent lab results, especially if there is a high index of suspicion. Blood, sputum (if pneumonic), bubo aspirates (if bubonic), and CSF (if meningitis) specimens should be obtained from patients with suspected plague.

Presumptive diagnosis:

- Appropriate clinical features (see right), are especially important in outbreak setting
- Staining of specimens: Gram-negative coccobacillus and bipolar-staining ("safety pin") on Wayson, Giemsa or Wright stains
- Several tests that aid in the confirmation of *Y. pestis* are available at reference laboratories, including enzyme-linked immunosorbent assay (ELISA) detection, direct immunofluorescence (DFA) and polymerase chain reaction (PCR).

Confirmatory diagnosis:

- Bacteriological: growth from specimen culture and subsequent analysis by a modern automated biochemical identification system. This generally requires at least 48 hours.
- Serological: Detection of anti-capsular antibodies by passive hemagglutination assay, either a $\geq$ 4 fold rise in titer from acute to (3-4 week) convalescent serum, or a single titer >1:128 in patients not previously vaccinated.



Histopathology of plague in human lung

Plague

Clinical Features of Plague

In all forms of plague, symptoms begin (incubation period 1-10 days) with a flu-like prodrome including fever, chills, myalgia, weakness, and headache. GI symptoms such as nausea, vomiting, diarrhea and abdominal pain are common. When death occurs, it is the result of sepsis, DIC and multiorgan failure.

Pneumonic plague: Chest discomfort, cough and dyspnea appear within 24 hours of prodrome onset. In contrast to inhalational anthrax, hemoptysis is often present and the CXR usually shows patchy, often bilateral, infiltrates and/or consolidation. By day 2-4 of illness, symptoms progress to cyanosis, respiratory distress and hemodynamic instability.

Primary and secondary pneumonic plague are similar in presentation, course of disease and required treatment.

Bubonic plague: Following inoculation, bacteria are transported to regional lymph nodes, which become swollen and painful (buboes) within 24 hours of prodrome onset. Rarely, an eschar or ulcer develops at the inoculation site, in contrast to tularemia.

Septicemic plague: Although 80% of bubonic plague cases develop bacteremia, <25% become secondarily septicemic. DIC, characterized by purpuric skin lesions and thrombosis that can cause acral gangrene, often develops late in the disease process followed by multiorgan failure. Meningitis occurs in 5% of cases.

Treatment

Treatment should be initiated as soon as a diagnosis of plague is suspected; do not delay for confirmatory testing. Untreated mortalities of 50% (bubonic) to nearly 100% (septicemic/pneumonic) can be reduced to <5% and 20-60%, respectively, if appropriate antibiotic therapy is initiated within 18-24 hours of symptom onset. Antibiotic resistance is rare in naturally-occurring plague, but could be a concern in a bioterrorism event.

Until sensitivities are known, treat as follows: continue treatment for 10 days (or 3 days after defervescence and clinical improvement), switching to oral therapy upon clinical improvement and the patient's ability to eat and absorb medications. Intensive supportive care will be required for severe cases.

- **Adults**
  streptomycin 1 g IM q 12 hrs (should be avoided in pregnant or lactating women) or
  gentamicin 2 mg/kg IV/IM load dose then 1–1.75 mg/kg IV/IM q 8 hrs per renal function
- **Children**
  streptomycin 15 mg/kg/day IM q 12 hrs (not to exceed 2g/day) or
  gentamicin 2.5 mg/kg IV/IM q 8 hrs (q 12 hrs for < 1 wk old or premature infants)

Alternative therapies include: doxycycline, tetracycline, ciprofloxacin, and chloramphenicol

- Chloramphenicol is the 1st choice for meningitis; avoid in pregnant or lactating women.

Noneffective therapies include: 3rd generation cephalosporins

In mass casualty incidents, parenteral administration may not be feasible; substitution with oral antibiotics, as recommended for post-exposure prophylaxis, may be necessary

Post-Exposure Prophylaxis

Prophylactic therapy for pneumonic plague is recommended from the first day of exposure and should be continued for 7 days past the date of the last exposure for the following:

- Those potentially exposed to aerosolized *Y. pestis* within the last 6 days
- All asymptomatic contacts (within 2 meters) of partially treated (<48 hrs of appropriate antibiotic) or untreated pneumonic plague patients

  Close contacts refusing prophylaxis and all persons receiving prophylaxis should be observed for 7 days post exposure and treated immediately with parenteral antibiotics if fever ≥ 38.3 C or cough develops (or tachypnea in infants)

Prophylax as follows:

- **Adults**

doxycycline 100 mg PO bid or
tetracycline 250 mg PO qid (should be avoided in pregnant or lactating women) or
ciprofloxacin 500 mg PO bid

- **Children**

doxycycline 2.2 mg PO bid for patients < 45 kg or
tetracycline 6.25-12.5 mg/kg PO qid; for patients ≥8 yrs or
ciprofloxacin 20 mg/kg PO bid; max: 1 g/day

Vaccination

Despite ongoing research, there is no vaccine currently available to the general public. A killed whole-cell vaccine was available in the US until 1998, when it was discontinued. Although it was very effective against bubonic plague, it required multiple injections and had little or no efficacy against pneumonic plague.

Original fact sheet and references available at www.bioterrorism.slu.edu

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Infection Control

Y. pestis is highly transmissible via respiratory droplets in patients with pneumonic plague; person to person transmission is rare in other forms of the disease.

Pneumonic plague:

Droplet isolation (private room or cohort confirmed cases, surgical mask & mask patient during transport). Discontinue isolation after 48 hrs of appropriate antibiotic therapy (consider culture sensitivity data if available) and patient demonstrates clinical improvement.

Bubonic or septicemic plague:

Standard precautions. If bubo is draining excessively, institute contact precautions (gown and gloves) until draining ceases.

All forms of plague:

Avoid surgery or other aerosol-generating procedures (including autopsies), or if necessary, wear proper respiratory protection (eg N-95 mask) and perform procedure in negative pressure room.

Only standard cleaning of patient rooms and handling of linens are necessary. Laboratory biosafety level 2 (BSL-2) precautions are adequate unless centrifuging, grinding or vigorous shaking (BSL 3 required).

Decontamination

Y. pestis is a relatively fragile organism and can remain viable for only 1 hour after an aerosol release. Environmental decontamination following aerosol release of plague is unnecessary. Standard hospital-approved disinfectants are adequate for cleaning patient rooms.

Reporting

Report suspected cases of *Y. pestis* or suspected intentional release of plague to your local health department. The local health department is responsible for notifying the state health department, FBI and local law enforcement. The state health department will notify the CDC.

Disclaimer

Information contained in this fact sheet was current as of March 2001, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment. *March 2001*